REMARKS

This is in response to the Office Action that was mailed on May 6, 2003. Claims 30, 36, 37, and 49 are amended to replace single letter codes for amino acids with the full names of the amino acids. Claims 30, 37, and 49 are amended to make subsections (a) consistent with the introductory portions of those claims. The amendment to claim 31 corrects a typographical error of omission, by which the amino acid sequence SEQ ID NO:10 was inadvertently omitted, resulting in a claim fragment that on its face clearly erroneously referred to a nucleic acid having e.g. an arginine at its second position. The correct full terminology was correctly set forth in claim 38 (which was treated by the Examiner in the same manner as claim 31 in item 9. on page 11 of the Office Action). Amendment of claim 31 in this manner is necessary to provide antecedent basis for the recitation of claim 32. Those of ordinary skill in the art would have recognized both the error and its correction. Claims 39 and 51 are amended to address a clarity issue raised by the Examiner. The specification is amended to correct a typographical error. No new matter is introduced by this Amendment, and no new issues are raised thereby. Therefore, entry of this Amendment in order to place the application into condition for allowance, or into better condition for appeal, is respectfully solicited. With this Amendment, claims 30-54 will remain in the application.

Regarding "priority", item 3. on page 2 of the Office Action, no claim for *foreign* priority has been made. However, a claim under 35 U.S.C. §119(e) to the benefit of U.S. provisional application Serial No. 60/106,426 has been made, and the Examiner is respectfully requested to acknowledge that claim in the item 14) on the Office Action Summary sheet.

Claims 30-54 were rejected as allegedly failing to satisfy the requirements of the second paragraph of 35 U.S.C. §112. Office Action, pages 10-11. Applicants' comments follow.

The Examiner alleges that claims 30, 37, and 49 are unclear with respect to their recitations of variants (a), (b), (c), *and/or* (d). It is respectfully submitted that the conjunction/disjunctive term "and/or" clearly extends, individually, to the limited group of embodiments (a), (b), (c), (d), (a)+(b), (a)+(c), (a)+(d), (b)+(c), (b)+(d), (c)+(d), (a)+(b)+(c), (a)+(b)+(d), (a)+(c)+(d), (b)+(c)+(d), and (a)+(b)+(c)+(d).

The Examiner questions, with respect to claim 30 and presumably with respect to claims 37 and 49, that it is unclear if the entire sequence can have conservative replacements. Applicants respectfully submit that it is clear that (i) only conservative replacements are contemplated, (ii) the amino acid sequence containing the conservative replacements must retain the biological activities of directing secretion of a fusion protein from a cell and cleavage of the secretory signal sequence from the fusion protein, *and* (iii) all conservative replacements must comply with rules (a)-(d).

Applicants agree with the Examiner that "and/or" in subsection (a) was unclear. Subsection (a) has been rewritten to recite the full names of amino acids formerly identified by single letter codes, and to reflect the fact that when G and D are both retained, there is no change from SEQ ID NO:10. Subsection (a) now clearly recites AD, VD, AE, VE, and GE as possible variants of GD.

Claim 36 has also been rewritten to eliminate single letter codes.

The Examiner questions the term "and/or" in claims 31 and 38. Here as elsewhere that terminology is used to indicate that all items listed or any subcombination of listed items (including a single item) are contemplated.

The Examiner questions the terminologies "desired heterologous protein" in claims 37 and 41 and "desired protein" in claim 48. Those skilled in the art would have no difficulty in understanding these terminologies in the context of the present invention. Moreover, the specification provides ample guidance as to the significance of these terminologies to the present invention. See for instance the specification, page 24, line 6 through page 27, line 12 for "desired protein" and page 27, line 13 through page 27, line 29 for "desired heterologous protein".

Claims 39 and 51 have been amended to overcome the dependency difficulties noted by the Examiner.

It is respectfully submitted that the claims as amended herein satisfy the requirements of the second paragraph of 35 U.S.C. §112.

Claims 30-54 were rejected as failing to satisfy the written description requirements of the first paragraph of 35 U.S.C. §112. Office Action, pages 3-6. Claims 30-54 were rejected on the ground of lack of enablement under the first paragraph of 35 U.S.C. §112. Office Action, pages 6-8. Claims 30-54 were rejected as including new matter. Office Action, pages 8-10. All of these rejections relate to the relationship between the claims herein and the underlying disclosure. Each of these grounds of rejection is respectfully traversed.

It is well settled that the statutory description and definiteness requirements may be met even if language in a claim does not appear in the specification. The Federal Circuit Court of Appeals so held in *All Dental Prodx LLC v. Advantage Dental Products Inc.*, 64 USPQ2d 1945 (Fed. Cir. 2002). The court stressed that the specification need not describe the invention in exactly the same terms as used in the claims to comply with the written description requirement. It must simply indicate to persons skilled in the art that, as of

the filing date, the applicant invented what is now recited in the claims. In the present situation, the language of the claims however actually paraphrases language from the specification, thus satisfying the "written description" and "no new matter" requirements of the statute.

Detailed and explicit relevant disclosure in the specification fully enables those skilled in the art to practice the invention claimed. See for instance the disclosure starting in line 29 on page 21 of the specification:

> The sequence MRVLVLALAVALAVGDQSNLG can be modified by amino acid replacements and by insertions or deletions from the sequence. The SS may have additional individual amino acids or amino acid sequences inserted into the polypeptide in the middle thereof and/or at the N-terminal and/or C-terminal ends thereof ***so long as the SS retains the biological activities of directing secretion of a fusion protein from a eukaryotic cell and cleavage of the secretory signal sequence from the fusion protein at a site between the G and D residues, or between any amino acids substituted for these positions***. Likewise, some of the amino acids may be deleted from the SS or substituted, so long as the resulting amino acid sequence retains those biological activities. Amino acid substitutions may also be made in the sequences so long as the polypeptide possesses the desired biological activities.
>
> ***The secretion activity of the SS can be arranged*** [sic, ***assayed***] ***by measuring the proportion of a reporter protein secreted into the medium of cultured recombinant cells expressing SS-reporter protein fusions. The cleavage activity can be assessed by N-terminal sequencing of the secreted protein.***
>
> One or more amino acid residues within the sequence can be substituted with another amino acid of similar polarity which acts as a functional equivalent, resulting in an altered polypeptide that retains the desired biological activities. Amino acid substitutions are preferably "conservative amino acid substitutions".
>
> ...
>
> [It] is preferable to retain a basic amino acid, preferably lysine or arginine, at the second residue of the SS. Also, it is preferred that the G and D residues constituting the cleavage site in the SS be retained; any substitution of these two amino acids is preferably A or V for the G and E for the D.

> Any integral number of additions or deletions of amino acids between 0 and 4 can be made to the SS; preferably only 1 or 2 additions or deletions are made. It is preferred that the stretch of hydrophobic amino acids in the interior of the SS be kept in the range 10-15 amino acids long, preferably 11-14, most preferably 11, 12 or 13 amino acids long.
>
> The number of substitutions that is tolerated is larger. An important aspect of the SS is that the hydrophobic stretch in its interior portion be retained. Many of the non-polar amino acids in this portion can be substituted with other non-polar amino acids, especially those having hydrocarbon side chains, without affecting the activity of the SS. Preferably fewer than 7 of the amino acids in the SS, more preferably fewer than 3, are substituted overall.

Specification, page 21, line 29 through page 23, line 31 (emphasis supplied).

Thus, certain variations are expressly set forth, and whether a particular amino acid satisfies the conditions of the claims can readily be determined by the methods mentioned above.

Claims 31, 38, and 50 are narrower in scope than claims 30, 37, and 49. Claims 31, 38, and 50 extend to only a handful of amino acid sequences, each of which can readily be conceptualized by those skilled in the art reading the claims and the supporting disclosure.

Claims 32, 33, 36, 39, 40, 51, and 52 all recite a single sequence! The Examiner has failed even to address these embodiments of Applicants' invention.

It is respectfully submitted that the claims presented herein satisfy all of the requirements of the first paragraph of 35 U.S.C. §112.

If the Examiner has any questions, she is asked to contact Mr. Richard Gallagher, (Reg. No. 28,781) at (703) 205-8008.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit

Account No. 02-2448 for any additional fees required under 37 CFR 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Mark J. Nuell
Reg. No. 36,623

DRN/RG

P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000